

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Incorporating Patient-Reported Outcomes into Shared Decision Making in the Management of Patients with Osteoarthritis of the Knee: A Hybrid Effectiveness-Implementation Study Protocol
AUTHORS	Lin, Eugenia; Uhler, Lauren; Finley, Erin; Jayakumar, Prakash; Rathouz, Paul; Bozic, KJ; Tsevat, Joel

VERSION 1 – REVIEW

REVIEWER	Tan, Bryan National Healthcare Group Woodlands Health Campus, Orthopaedic Surgery
REVIEW RETURNED	20-Aug-2021

GENERAL COMMENTS	<p>Thank you for inviting me to review this very interesting study protocol looking at the effectiveness of a PROM guided, AI-enabled decision-making tool for knee arthroplasty while concurrently looking at the implementation through interviews with both patients and healthcare providers via a mixed method approach and effectiveness-implementation hybrid trial. Such tools are much needed in today's healthcare world where personalized and precision medicine is the new frontier, partnering patients and tailoring treatments to suit their needs and preferences to deliver value-based care. I look forward to the results of this study.</p> <p>Just a couple of comments/observations about the protocol for the authors to consider</p> <ol style="list-style-type: none">1. As an overall observation, it would be good to format the information presented and reference the SPIRIT checklist to ensure that all critical information is present as part of the trial protocol. For example, more information about the data collection methods and intervention would have been useful.2. The study is planned to be conducted over 2 sites that have very different practices, care team, established modes of assessment (PROMs etc) and patient population. This might pose a challenge in terms of the trial evaluation.3. Joint Insights validity. What population's data was its development was based on? How does it differ in the study population or is it the same population?4. Sample Size Calculation – how was it calculated for qualitative interviews?5. Why non-blinding? Can single-blinding be considered with the outcome assessors blinded?
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	<p>6. With regards to the intervention itself, the primary difference appears to be the predicted risk-benefit ratio for a knee replacement surgery as a subset of the Joint Insight program while the control arm will still get the educational component and value/preference elicitation portion of the program. Instead of testing a specific component of Joint Insight program, would it be feasible or potentially easier to assess Joint Insight program as a whole vs standard counselling?</p> <p>7. Would the inclusion criteria for patients who have been assessed by an Orthopaedic surgeon and subsequently offered/recommended surgery to be a better population to test this Joint Insight program since a key component is specifically the risk-benefit ratio of surgery. From the protocol, I note there is a pre-clinic huddle to identify suitable patients and patients are recruited into the study prior the consultation with the surgeon. There may be a situation where the surgeon upon assessment deems the patient not suitable for surgery for a variety of reasons and such a surgery specific decision-making tool such as Joint Insight tool may not be relevant. The patient unfortunately would already have been consented and randomized into the study.</p> <p>8. In order to balance what is delivered in both the control and intervention arm, would the authors consider a standardized script of information that will be delivered by the attending surgeon for both the intervention and control arm to ensure that any difference seen would be due to the Joint Insight program?</p>
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REVIEWER	Migliorini, Filippo University Hospital RWTH Aachen, Orthopedics
REVIEW RETURNED	21-Sep-2021

GENERAL COMMENTS	<p>Thank you for considering me as Revisor for the following manuscript entitled "Incorporating Patient-Reported Outcomes into Shared Decision Making in the Management of Patients with Osteoarthritis of the Knee: A Hybrid Effectiveness-Implementation Study Protocol Paper"</p> <p>The manuscript is well written. I have only few suggestions</p> <p>Please substitute paper with article or study</p> <ul style="list-style-type: none"> -Please moderate this sentence in the abstract: "Treatment for knee OA includes nonsurgical treatments and total knee replacement (TKR), which can often alleviate pain and restore physical function, but is expensive and inappropriately performed in up to a third of patients based on guidelines" -once you use the abbreviations, please continue to use that abbreviation -please use the third person in the whole manuscript -please delete surgery after TKR -please write the number from 0 to 10 in words
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REVIEWER	HONVO, Germain University of Liege, Division of Public Health, Epidemiology and Health Economics
REVIEW RETURNED	27-Sep-2021

GENERAL COMMENTS	<p>Title: Incorporating Patient-Reported Outcomes into Shared Decision Making in the Management of Patients with Osteoarthritis of the Knee: A Hybrid Effectiveness- Implementation Study Protocol Paper</p> <p>Journal: BMJ Open</p> <p>Peer review round (date): 27/09/21</p> <p>Recommendation: Minor revision</p> <p>Comments to authors</p> <p>The reviewer congratulates the authors for this important initiative for better management of patients with osteoarthritis of the knee. Here are some comments/questions to improve the reporting of this protocol.</p> <p>Abstract:</p> <p>Please move the aim statement from the Methods section to the end of Introduction.</p> <p>The reviewer suggests changing "Aim 1" and "Aim 2" to "Part 1 or Sub-study 1" and "Part 2 or Sub-study 2" or to something similar (but avoid stating "Aim 1 consists of..." and "In Aim 2...").</p> <p>In the current "Aim 1", what is the difference between "clinical effectiveness" and "impact" in this specific context? Will "impact" be really measured in the current study?</p> <p>Why did the authors use different tenses for description of part 1 and part 2 of the study? Please check and harmonize where necessary.</p> <p>If possible, please add a sub-section on "expected results" (based on the hypotheses formulated), both in the Abstract and in the full manuscript.</p> <p>Under "Ethics and Dissemination", the authors stated that the study was "registered with Clinicaltrials.gov". If only part 1 of the study has been registered, please amend this statement.</p> <p>Background</p> <p>The three first paragraphs of the introduction (page 5-6) are well-written and clear. However, the reviewer was quite lost when reading paragraphs 4-6 (page 6, line 19 to page 7). The reviewer suggests to the authors to shorten this part and make clear to the reader the link between previous findings and the current research. In other terms, please make clear in quite few words why this study is important to be undertaken.</p> <p>Methods and analysis</p> <p>Regarding Aim 1, how will "decision quality" be assessed?</p> <p>In Aim 2, there is something going wrong here: "to implement and evaluate the feasibility...". Please check and rephrase Aim 2, keeping in mind to make it clear for readers.</p> <p>What is the interest of implementing the tool in a patient population (Aim 2) different from population for Aim 1? What is the difference between these two populations? Please consider briefly explaining this in the methods section.</p> <p>The authors provided description of two healthcare centers without stating which center will be considered for what sub-study.</p>
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	<p>Moreover, it would be good to point out differences/similarities in these two centers and explain why these have been chosen and not others, instead of simply describing them.</p> <p>The “Joint Insights” tool has been deservedly described in the methods section. The reviewer wonders why this has also been done in the introduction. The description provided in the introduction may be moved to the methods section. Otherwise, please clarify the need of the current choice.</p> <p>To ease understanding of this protocol to readers, the reviewer suggests reporting first the full methods for sub-study 1 (Aim 1), then methods for sub-study 2 (Aim 2), all under a unique Methods section. The reviewer suggests to the authors to consider paying attention to clarity and concision while describing each part of the Methods section. Please avoid long sentences.</p> <p>Statistical analyses: Please consider describing sample size calculation before reporting how data will be analysed.</p> <p>Please consider using the right tense (for verbs) for protocol description.</p> <p>1</p>
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REVIEWER	Bowden, Jocelyn The University of Sydney, Institute of Bone and Joint Research
REVIEW RETURNED	01-Oct-2021

GENERAL COMMENTS	<p>Dear study authors</p> <p>Thank you for your protocol. You are undertaking a hybrid study to assess the clinical effectiveness and implementation of a new tool to guide shared decision making with knee OA patients. Your project will use a machine learning-based approach to integrate PROMs and clinical variables into the tool, to assist patient decision making in different health care settings. This is a very interesting study, with a well written background. I do have a few comments on your protocol, mainly around clarity of the methods and reporting requirements. You may wish to revisit the STROBE/CONSORT guidelines and include any missing items.</p> <p>Main comments:</p> <ol style="list-style-type: none"> 1. For the international audience, please mention in the abstract and main text that the trial is being undertaken in the US. 2. Please include the version number of the protocol that was registered. 3. Recruitment: is the researcher part of the clinical team, or are they independent? 4. Inclusion criteria: please add an interpretation of the KOOS scores listed (e.g. 0=??) 5. Study setting: I'm sorry if I've missed it but can you please include a short description in this section of why patients are referred to each of the clinics (are they referred for OA management in general or as an assessment for surgery?), and if they are on referred or can they self-nominate to attend? 6. For the RCT, do you have criteria for discontinuing or modifying the protocols (e.g. do you have DMC?), measuring adherence, or interim analysis guidelines?
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	<p>7. Outcomes: You have stated the primary outcome, but not the primary timepoint. Is it 3 or 6 months? A separate table that summarises the timepoints and outcome measures would be helpful. Please also include more detail on the outcome measures (e.g. scales used and anchor points,</p> <p>8. Similarly, a figure with anticipated patient time-lines would also assist interpretation. Figures 1 and 2 are great overviews, but more detail around timeframes, and how long each of these sections would be helpful.</p> <p>9. Please include the anticipated dates (start, finish, recruitment etc) for the study.</p> <p>10. Please include an anticipated flow diagram for the RCT, including the enrolment, allocation, intervention, enrolment, intervention and followup phases (as applicable).</p> <p>11. Who will actually inform people of the group allocation? Is it the same person as who performs the randomisation?</p> <p>12. What are your plans for people who withdraw (e.g. do you keep all of their data to that point)?</p> <p>13. Please include a statement on collection of AE and SAE data.</p> <p>14. Optional - As you are undertaking an implementation trial, you may wish to think about wider dissemination avenues (in addition to the usual ones you have listed), and how you will get uptake for your results in clinical practice.</p> <p>15. Do you have any references for your sample size calculations?</p> <p>16. please state in the manuscript that the study was prospectively registered.</p> <p>17. its appears from your protocol registration that you have started recruitment. Please confirm the dates that recruitment commenced.</p> <p>Minor comments: Page 6, line 40. Missing a full stop. Page 8, line 37. Perhaps use the future tense here (suitable patients will be...) Page 9, line 41. Need a capital letter for 'our'.</p>
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REVIEWER	Park, Yeonhee University of Wisconsin-Madison, Biostatistics and Medical Informatics
REVIEW RETURNED	02-Oct-2021

GENERAL COMMENTS	<p>1. Title says a hybrid study, but it evaluates the clinical effectiveness based on RCT study only and investigates the implementation of the patient decision aid separately. Simultaneous or seamless combining Aim 2 and 1 would improve the patient health outcome for the hybrid trial.</p> <p>2. More interesting part is Aim 2, but statistical analysis plan (SAP) is weak (e.g., tool evaluation and investigation of impact). It mentions evaluation of adaptations and barriers and facilitators,</p>
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	<p>but it is hard to know the specific plans to analyze the data for them. Integration model using RCT data and data for periodic reflection, semi-structured interviews, and EHR data should be described and well planned. This paper mainly provides some SAP for Aim 1.</p> <p>3. It does not include the validation of model assumption or model evaluation in SAP. Some secondary endpoint is longitudinal, and the longitudinal data may need to fit the data with a certain model depending on the study objective, which is not clear.</p> <p>4. Since it uses EHR database, authors should raise and address the challenging issues of the EHR.</p> <p>5. It would be better to display the proposed hybrid study including clinical data and PRO measure. This will be helpful to understand the hybrid study.</p> <p>6. Since this study already started to recruit, some more description can be provided for the patient and public involvement in terms of design and feedback of the tool.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Bryan Tan, National Healthcare Group Woodlands Health Campus Comments to the Author:

Thank you for inviting me to review this very interesting study protocol looking at the effectiveness of a PROM guided, AI-enabled decision-making tool for knee arthroplasty while concurrently looking at the implementation through interviews with both patients and healthcare providers via a mixed method approach and effectiveness-implementation hybrid trial. Such tools are much needed in today's healthcare world where personalized and precision medicine is the new frontier, partnering patients and tailoring treatments to suit their needs and preferences to deliver value-based care. I look forward to the results of this study.

Just a couple of comments/observations about the protocol for the authors to consider

Reviewer 1 comment:

1. As an overall observation, it would be good to format the information presented and reference the SPIRIT checklist to ensure that all critical information is present as part of the trial protocol. For example, more information about the data collection methods and intervention would have been useful.

Author response: Thank you for your suggestion. A SPIRIT checklist has been added. We have added more information about data collection methods. The following has been added to the Methods (page 10): "Demographic information is collected after randomization via tablets. Next, patients in the intervention group receive a Joint Insights risk/benefit report. Those randomized to the intervention group may review and discuss the Joint Insights report as part of the clinical visit. The control group does not receive the Joint Insights report. Following the completion of the visit, survey instruments are collected for participants in both arms by using REDCap forms on the tablet. At 3-months and 6-months follow-up, participants are given follow-up surveys on REDCap either in person, by email, or by phone. Participants completing follow-up survey receive a \$25 gift card."

Reviewer 1 comment:

2. The study is planned to be conducted over 2 sites that have very different practices, care team, established modes of assessment (PROMs etc) and patient population. This might pose a challenge in terms of the trial evaluation.

Author response: Thank you for the feedback. The first aim, the randomized controlled trial, will take place completely at one site. The second aim, the implementation study using qualitative analysis, will take place at the second site. We believe this is a significant strength of the study, as it will allow us to conduct pragmatic evaluation of implementation feasibility and acceptability in a second site with unique population, electronic health record, and clinical model/organization. The resulting implementation data will be of immense value in planning for future research, scale-up and spread of the intervention.

Reviewer 1 comment:

3. Joint Insights validity. What population's data was its development was based on? How does it differ in the study population or is it the same population?

Author response: Details of the data informing Joint Insights are found in Methods (page 6): "Patient journeys are drawn from the OM1 Intelligent Data Cloud (OM1, Inc., Boston, MA) for patients undergoing TKR who have adequate follow-up for the outcome being evaluated. Approximately 675,000 patients' records were used for the original risk model, which continues to be updated. 60.8% of the modeling population (risk model) patients are male, the mean age is 65 years, and the mean body mass index is 31.8 kg/m²." Based on our previous trial [Jayakumar JAMA Network Open 2021], we expect our study population will be slightly more female (approximately 65%), similar in age (mean approximately 62 years), and with a similar mean BMI (approximately 33).

Reviewer 1 comment:

4. Sample Size Calculation – how was it calculated for qualitative interviews?

Author response: The Reviewer asks an important question. To ensure the manuscript better addresses this point, we have added the following to the Methods section, page 15: "For staff and provider interviews, we have invited every member of the clinical team to participate in order to have full representation of those involved in implementation. In developing our patient sample, we considered the need to capture heterogeneity in patient demographics, condition severity, need for surgery, health literacy, and preferences for treatment planning, while also acknowledging the relative homogeneity of the patient population being evaluated for knee replacement surgery in a single orthopedic clinic. Following recommendations for ensuring information power, as specified by Malterud et al. (2006), we therefore estimated that a sample of 25 patients at each time point would provide adequate information power to represent a broad range of patient experiences and perspectives."

Reviewer 1 comment:

5. Why non-blinding? Can single-blinding be considered with the outcome assessors blinded?

Author response: Thank you for your question. Non-blinding is essential to both patients and providers due to the discussion that the PDA elicits and accompanies through the use of the tool. Logistically, non-blinding is also essential for research associates to provide the inputs and outputs of the tool itself. However, single-blinding can be considered with the outcome assessors blinded, and we will make this consideration.

Reviewer 1 comment:

6. With regards to the intervention itself, the primary difference appears to be the predicted risk-benefit ratio for a knee replacement surgery as a subset of the Joint Insight program while the control arm will still get the educational component and value/preference elicitation portion of the program. Instead of testing a specific component of Joint Insight program, would it be feasible or potentially easier to assess Joint Insight program as a whole vs standard counselling?

Author response: Thank you for this suggestion. While assessing Joint Insights as a whole vs standard care would be another interesting study, we have chosen to focus on the specific effect of the risk/benefit report. We wanted to give the control group some information and if we find an effect of the risk/benefit report, that would be stronger evidence of the effectiveness of using PROMs for personalized outcome prediction.

Reviewer 1 comment:

7. Would the inclusion criteria for patients who have been assessed by an Orthopaedic surgeon and subsequently offered/recommended surgery to be a better population to test this Joint Insight program since a key component is specifically the risk-benefit ratio of surgery. From the protocol, I note there is a pre-clinic huddle to identify suitable patients and patients are recruited into the study prior the consultation with the surgeon. There may be a situation where the surgeon upon assessment deems the patient not suitable for surgery for a variety of reasons and such a surgery specific decision-making tool such as Joint Insight tool may not be relevant. The patient unfortunately would already have been consented and randomized into the study.

Author response: Thank you for your thoughtful question and assessment. Inclusion criteria (page 10) were selected so that only patients who are surgical candidates are enrolled.

Reviewer 1 comment:

8. In order to balance what is delivered in both the control and intervention arm, would the authors consider a standardized script of information that will be delivered by the attending surgeon for both the intervention and control arm to ensure that any difference seen would be due to the Joint Insight program?

Author response: Thank you for your suggestion. This is a pragmatic clinical trial intended to allow the surgeon to discuss treatment options with the patient as they normally would.

Reviewer: 2

Dr. Filippo Migliorini, University Hospital RWTH Aachen

Comments to the Author:

Thank you for considering me as Revisor for the following manuscript entitled "Incorporating Patient-Reported Outcomes into Shared Decision Making in the Management of Patients with Osteoarthritis of the Knee: A Hybrid Effectiveness-Implementation Study Protocol Paper"

The manuscript is well written. I have only few suggestions

Reviewer 2 comment:

Please substitute paper with article or study

Author response: Thank you for your feedback. We have changed the title to the following: Incorporating Patient-Reported Outcomes into Shared Decision Making in the Management of Patients with Osteoarthritis of the Knee: A Hybrid Effectiveness-Implementation Study Protocol

Reviewer 2 comment:

Please moderate this sentence in the abstract: "Treatment for knee OA includes nonsurgical treatments and total knee replacement (TKR), which can often alleviate pain and restore physical function, but is expensive and inappropriately performed in up to a third of patients based on guidelines"

Author response: Thank you for your suggestion. We edited the sentence (page 2) to say: "The primary surgical treatment of knee OA is total knee replacement (TKR), a procedure that aims to

alleviate pain and restore physical function. However, TKR is expensive and, based on professional guidelines, inappropriately performed in up to a third of patients.” Although we cannot add the citation to the abstract, this sentence is supported by the following citation which is noted in the Background section: Riddle DL, Jiranek WA, Hayes CW. Use of a validated algorithm to judge the appropriateness of total knee arthroplasty in the United States: a multicenter longitudinal cohort study. *Arthritis & rheumatology*. 2014 Aug;66(8):2134-43.

Reviewer 2 comment:

once you use the abbreviations, please continue to use that abbreviation

Author response: We appreciate this review. We have amended this article to use abbreviations following introduction of abbreviation.

Reviewer 2 comment:

please use the third person in the whole manuscript

Author response: Thank you for this suggestion. We believe this is a matter of style and prefer to use first person in some instances.

Reviewer 2 comment:

please delete surgery after TKR

Author response: This has been amended throughout the article.

Reviewer 2 comment:

please write the number from 0 to 10 in words

Author response: Thank you, we have chosen to use AMA style guidelines which specify use of numerals for numbers and have continued with this stylistic formatting.

Reviewer: 3

Dr. Germain HONVO, University of Liege

Comments to the Author:

The reviewer congratulates the authors for this important initiative for better management of patients with osteoarthritis of the knee. Here are some comments/questions to improve the reporting of this protocol.

Reviewer 3 comment:

Abstract:

1. Please move the aim statement from the Methods section to the end of Introduction.

Author response: Thank you for your suggestion. This has been amended (page 2).

Reviewer 3 comment:

2. The reviewer suggests changing “Aim 1” and “Aim 2” to “Part 1 or Sub-study 1” and “Part 2 or Sub-study 2” or to something similar (but avoid stating “Aim 1 consists of...” and “In Aim 2...”).

Author response: Thank you for your feedback. We have edited the text to refer to Sub-study 1 and Sub-study 2 per your suggestion and appreciate the clarity it provides for this article.

Reviewer 3 comment:

3. In the current “Aim 1”, what is the difference between “clinical effectiveness” and “impact” in this specific context? Will “impact” be really measured in the current study?

Author response: We appreciate this commentary. We have amended the abstract (page 2) and aims statement (pages 5-6) to include only clinical effectiveness: “Aim 1: To evaluate the clinical effectiveness of the PRO-guided predictive analytic Joint Insights tool and process in terms of decision quality and treatment choice for patients with knee OA.”

Reviewer 3 comment:

4. Why did the authors use different tenses for description of part 1 and part 2 of the study? Please check and harmonize where necessary.

Author response: Thank you for your review of this. We have used the appropriate tense based on what has been accomplished so far.

Reviewer 3 comment:

5. If possible, please add a sub-section on “expected results” (based on the hypotheses formulated), both in the Abstract and in the full manuscript.

Author response: We added a section on Expected Results on page 17: “Sub-study 1: We expect that patients who used the full Joint Insights tool will have higher decision process scores, reflecting better decision quality, compared with those who saw the education and preferences modules only. We also expect patients in the intervention group to report higher levels of SDM and lower levels of decision conflict and decision regret. We don’t expect a difference in rates of treatment selected (operative vs. non-operative) between the two groups.”

Sub-study 2 is exploratory in nature and thus has no formal hypotheses.

Reviewer 3 comment:

6. Under “Ethics and Dissemination”, the authors stated that the study was “registered with Clinicaltrials.gov”. If only part 1 of the study has been registered, please amend this statement.

Author response: We have edited the text to note that only sub-study 1 was registered under the subheader Trial Registration (page 3).

Reviewer 3 comment:

Background

7. The three first paragraphs of the introduction (page 5-6) are well-written and clear. However, the reviewer was quite lost when reading paragraphs 4-6 (page 6, line 19 to page 7). The reviewer suggests to the authors to shorten this part and make clear to the reader the link between previous findings and the current research. In other terms, please make clear in quite few words why this study is important to be undertaken.

Author response: Thank you for the suggestion to make our Background section more succinct. We have deleted paragraphs 4-6 and have edited the introduction to provide additional clarity and emphasize the importance of the current study (pages 3-5).

Reviewer 3 comment:

Methods and analysis

8. Regarding Aim 1, how will “decision quality” be assessed?

Author response: Decision quality will be assessed using the previously validated Decision Process sub-score of the Decision Quality Index as described in the Methods (page 8).

Reviewer 3 comment:

9. In Aim 2, there is something going wrong here: “to implement and evaluate the feasibility...”. Please check and rephrase Aim 2, keeping in mind to make it clear for readers.

Author response: We edited Aim 2 (page 5) to read: “In a qualitative assessment at the second site, to implement and evaluate the feasibility and acceptability of the tool and SDM process in a second clinical setting with a different clinical population, provider group, and EHR by using principles of behavior design and intervention mapping.”

Reviewer 3 comment:

10. What is the interest of implementing the tool in a patient population (Aim 2) different from population for Aim 1? What is the difference between these two populations? Please consider briefly explaining this in the methods section.

Author response: We have added the following text to the Methods (page 6) under a new sub-header Study Dates and Sites: “The decision aid has already been integrated into the workflow of the UT Health Austin clinic, where the effectiveness trial (Sub-study 1) is taking place. The study design and choice of different setting (UT Health San Antonio) for the implementation study (Sub-study 2) is intentional to allow for further understanding of the feasibility and acceptability of implementing the tool into a clinic with a different population, care delivery model having less familiarity with using PROS routinely in practice, and a different EHR (Table 1).”

Reviewer 3 comment:

11. The authors provided description of two healthcare centers without stating which center will be considered for what sub-study. Moreover, it would be good to point out differences/similarities in these two centers and explain why these have been chosen and not others, instead of simply describing them.²

Author response: We have added additional details under Study Dates and Sites (page 7) and in a new table (Table 1) to highlight differences and similarities between sites and further explain reasons for choosing each site.

Reviewer 3 comment:

12. The “Joint Insights” tool has been deservedly described in the methods section. The reviewer wonders why this has also been done in the introduction. The description provided in the introduction may be moved to the methods section. Otherwise, please clarify the need of the current choice.

Author response: The description has been deleted in the introduction section.

Reviewer 3 comment:

13. To ease understanding of this protocol to readers, the reviewer suggests reporting first the full methods for sub-study 1 (Aim 1), then methods for sub-study 2 (Aim 2), all under a unique Methods section. The reviewer suggests to the authors to consider paying attention to clarity and concision while describing each part of the Methods section. Please avoid long sentences.

Author response: Thank you for your feedback regarding this clarification. We have amended the article to reflect first the full methods of sub-study 1, and then sub-study 2.

Reviewer 3 comment:

14. Statistical analyses: Please consider describing sample size calculation before reporting how data will be analysed.

Author response: The paragraphs describing sample size calculations (pages 11 and 16) have been moved to appear before analysis plans.

Reviewer 3 comment:

15. Please consider using the right tense (for verbs) for protocol description.

Author response: We appreciate your suggestion. We have amended this throughout the article.

Reviewer: 4

Dr. Jocelyn Bowden, The University of Sydney Comments to the Author:

Dear study authors

Thank you for your protocol. You are undertaking a hybrid study to assess the clinical effectiveness and implementation of a new tool to guide shared decision making with knee OA patients. Your project will use a machine learning-based approach to integrate PROMs and clinical variables into the tool, to assist patient decision making in different health care settings. This is a very interesting study, with a well written background. I do have a few comments on your protocol, mainly around clarity of the methods and reporting requirements. You may wish to revisit the STROBE/CONSORT guidelines and include any missing items.

Reviewer 4 comment:

Main comments:

1. For the international audience, please mention in the abstract and main text that the trial is being undertaken in the US.

Author response: Thank you for your feedback. We have included this information in the abstract (page 2).

Reviewer 4 comment:

2. Please include the version number of the protocol that was registered.

Author response: This information was added to Trial Registration (page 3): "Sub-study 1 (protocol version 1.2, dated 2 February 2021) was prospectively registered with Clinicaltrials.gov (NCT04805554) on 18 March 2021."

Reviewer 4 comment:

3. Recruitment: is the researcher part of the clinical team, or are they independent?

Author response: Thank you for your question. The researchers are not part of the clinical team other than Dr. Kevin Bozic, who is an orthopaedic surgeon seeing patients at the UT Health Austin. Under Participant Recruitment and Data Collection (page 10), we added Dr. Bozic's initials after Provider A to show he is also an orthopaedic surgeon seeing patients enrolled in this study.

Reviewer 4 comment:

4. Inclusion criteria: please add an interpretation of the KOOS scores listed (e.g. 0=??)

Author response: The following text has been added to the Methods (pages 6-7): “The KOOS JR is a 7-item PROM encompassing questions on function, pain, and stiffness and scored using a t-score from zero to 100, where 100 represents best knee health and zero the poorest.”

Reviewer 4 comment:

5. Study setting: I’m sorry if I’ve missed it but can you please include a short description in this section of why patients are referred to each of the clinics (are they referred for OA management in general or as an assessment for surgery?), and if they are on referred or can they self-nominate to attend?

Author response: We’ve added the following text to Participant Recruitment and Data Collection, page 10: “The UT Health Austin Musculoskeletal Institute sees a mix of patients seeking care for knee OA. This includes cases with a range of pathological severity, and individuals who are referred from primary or specialty care or self-referred.” and page 15: “The MARC Orthopaedics Clinic in San Antonio sees a mix of patients seeking care for knee OA or considering TKR, and a mix of patients who are referred or self-referred.”

Reviewer 4 comment:

6. For the RCT, do you have criteria for discontinuing or modifying the protocols (e.g. do you have DMC?), measuring adherence, or interim analysis guidelines?

Author response: We do not have a Data Monitoring Committee since the study is low risk to the patients. Regarding adherence, we will assess and record whether the Joint Insights tool was actually used. Then, as we have stated, “additional analyses will follow the “per-protocol” principle wherein the main treatment variable will be whether the Joint Insights tool was actually used.” There are no interim analyses planned. Data will be analyzed after all participants have completed their participation in the study.

Reviewer 4 comment:

7. Outcomes: You have stated the primary outcome, but not the primary timepoint. Is it 3 or 6 months? A separate table that summarises the timepoints and outcome measures would be helpful. Please also include more detail on the outcome measures (e.g. scales used and anchor points,

Author response: We have included the primary timepoint in the Methods section (page 7): “Quantitative outcomes include the primary endpoint decision quality – as assessed at the conclusion of the initial consultation by using the previously validated Decision Process sub-score of the Decision Quality Index (DQI) for knee OA.” Figure 2 summarizes data and outcome measures collected at each timepoint (baseline visit pre- and post-consultation, 3 month follow-up and 6 month follow-up). We’ve added additional information about the outcome measures to the Figure legend, page 22.

Reviewer 4 comment:

8. Similarly, a figure with anticipated patient time-lines would also assist interpretation. Figures 1 and 2 are great overviews, but more detail around timeframes, and how long each of these sections would be helpful.

Author response: We’ve tried to capture this information in Figure 2.

Reviewer 4 comment:

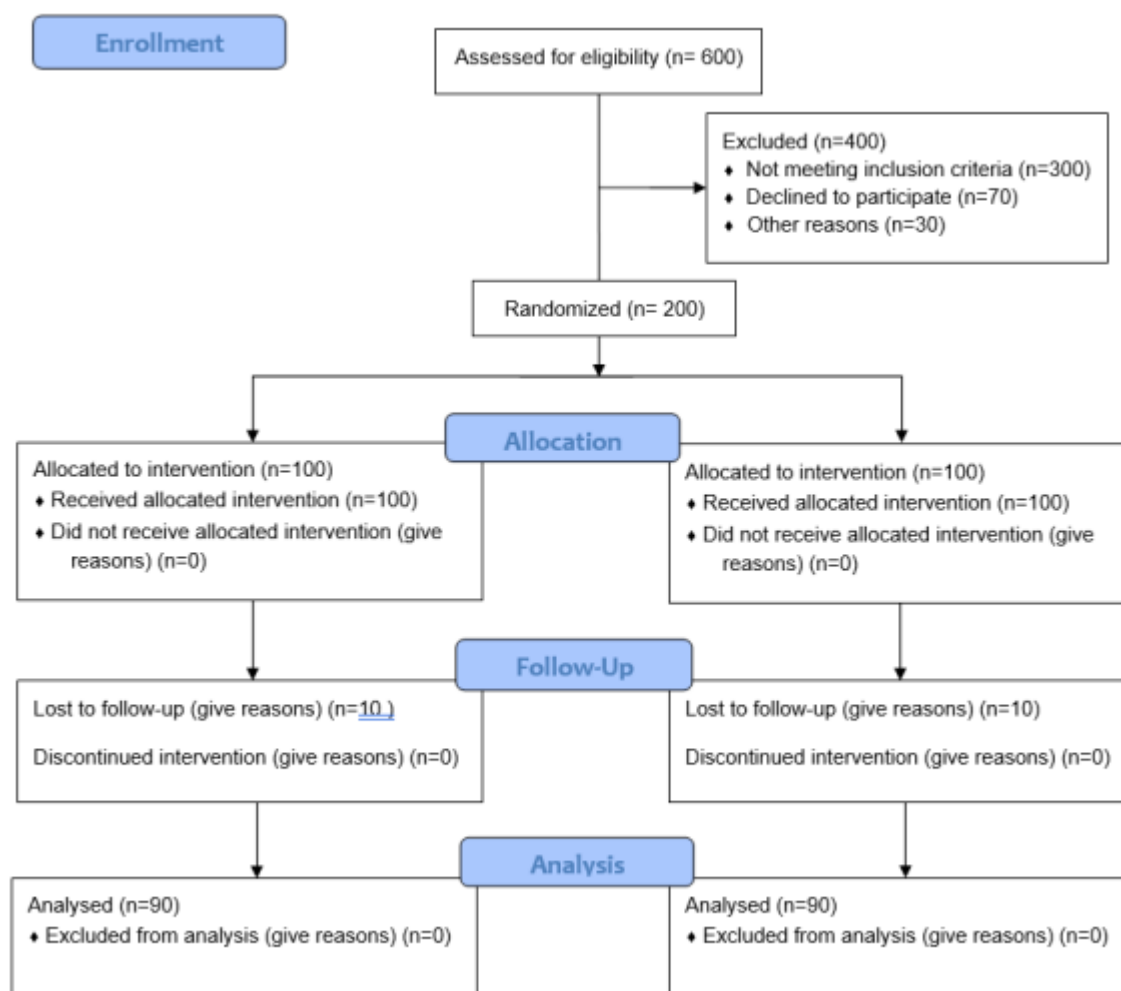
9. Please include the anticipated dates (start, finish, recruitment etc) for the study.

Author response: The dates for study start, recruitment start, and anticipated study end have been added to the Study Dates and Sites section, page 7.

Reviewer 4 comment:

10. Please include an anticipated flow diagram for the RCT, including the enrolment, allocation, intervention, enrolment, intervention and followup phases (as applicable).

Author response: We have included below an anticipated flow diagram to further clarify the anticipated phases of the RCT.



Reviewer 4 comment:

11. Who will actually inform people of the group allocation? Is it the same person as who performs the randomisation?

Author response: Thank you for your question. The same person who informs people of group allocation is the same person who performs the randomization.

Reviewer 4 comment:

12. What are your plans for people who withdraw (e.g. do you keep all of their data to that point)?

Author response: The intervention occurs entirely on the baseline day. Withdrawal leading to missingness of any data collected at baseline will be minimal. Subjects declining to participate at the 3- or 6-month timepoints will still be included in analyses by analyzing their data in the context of linear mixed models (Fitzmaurice, G. M., Laird, N. M., & Ware, J. H. 2012. Applied longitudinal analysis. Vol. 998. John Wiley & Sons.) for continuous outcomes or weighted GEE, allowing for

dropout (Preisser, J. S., Lohman, K. K., & Rathouz, P. J. 2002. Performance of weighted estimating equations for longitudinal binary data with drop-outs missing at random. *Statistics in medicine*, 21(20), 3035-3054.) for binary outcomes. These missing data methods exploit earlier outcomes (e.g., at baseline) and the correlation between the 3 timepoints to make valid inferences for 3- and 6-month endpoints.

Reviewer 4 comment:

13. Please include a statement on collection of AE and SAE data.

Author response: Thank you for your suggestion. We have added the following under Ethics and Dissemination (page 17): "Although we don't anticipate any adverse events, any adverse events will be reported to the local IRB."

Reviewer 4 comment:

14. Optional – As you are undertaking an implementation trial, you may wish to think about wider dissemination avenues (in addition to the usual ones you have listed), and how you will get uptake for your results in clinical practice.

Author response: If this study is successful, we plan to do another study with additional, more heterogeneous sites.

Reviewer 4 comment:

15. Do you have any references for your sample size calculations?

Author response: Sample size and power were estimated using the `_power twomeans_` function in Stata (StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC.).

Reviewer 4 comment:

16. please state in the manuscript that the study was prospectively registered.

Author response: Thank you for your suggestion. We have added this statement to Trial Registration (page 3).

Reviewer 4 comment:

17. its appears from your protocol registration that you have started recruitment. Please confirm the dates that recruitment commenced.

Author response: We have added the recruitment start date of this study (22 February 2021) into the manuscript (page 7).

Reviewer 4 comment:

Minor comments:

Page 6, line 40. Missing a full stop.

Page 8, line 37. Perhaps use the future tense here (suitable patients will be...)

Page 9, line 41. Need a capital letter for 'our'.

Author response: Thank you for these minor comments. These have been amended in the protocol article.

Reviewer: 5

Reviewer 5 comment:

1. Title says a hybrid study, but it evaluates the clinical effectiveness based on RCT study only and investigates the implementation of the patient decision aid separately. Simultaneous or seamless combining Aim 2 and 1 would improve the patient health outcome for the hybrid trial.

Author response: We agree that it would be ideal to integrate patient health outcomes and assess acceptability and feasibility of implementation at the same site as the Reviewer suggests. Unfortunately, this is not possible in the current study, given that one site is significantly further along in implementation and adoption of the patient decision aid. And yet, there are advantages to studying implementation at a new site. In contrast to the first site, the second site is in the early stages of implementation and therefore offers an appropriate context in which to explore acceptability and feasibility of the tool in a novel setting. Both clinical effectiveness and implementation data are of immediate value in furthering the science regarding potential for impact in scaling this intervention more broadly.

Reviewer 5 comment:

2. More interesting part is Aim 2, but statistical analysis plan (SAP) is weak (e.g., tool evaluation and investigation of impact). It mentions evaluation of adaptations and barriers and facilitators, but it is hard to know the specific plans to analyze the data for them. Integration model using RCT data and data for periodic reflection, semi-structured interviews, and EHR data should be described and well planned. This paper mainly provides some SAP for Aim 1.

Author response: We are grateful that the Reviewer appreciates the value of sub-study 2's investigation of implementation process and outcomes (e.g., feasibility, acceptability) for the decision aid. There is no formal statistical analysis plan for sub-study 2 as all quantitative patient data will be descriptive; the qualitative analytic plan is now described in greater detail on page 16. All qualitative data regarding implementation processes, events, and multi-stakeholder perspectives will be integrated as described to inform future refinement, scale-up and spread of the decision aid in future research, should the clinical effectiveness data from sub-study 1 suggest this intervention is of clear benefit for patients.

Reviewer 5 comment:

3. It does not include the validation of model assumption or model evaluation in SAP. Some secondary endpoint is longitudinal, and the longitudinal data may need to fit the data with a certain model depending on the study objective, which is not clear.

Author response: As described below, both the models for the mean response and the models for the association among repeated measures will be fully saturated, so model misspecification risk will be minimal. Should the responses deviate substantially from normality (for continuous response), response transformations will be used to ensure similar directions and strengths of effects, and strong differences will be reported. Sensitivity to outliers, if any, will be assessed via Cook's D measure and reported (but such observations will not be excluded from analysis unless we find errors in those measures).

The following was added to the Quantitative Analysis section, page 11: "For analysis of the 3- and 6-month data, we will fit linear mixed models (Fitzmaurice, G. M., Laird, N. M., & Ware, J. H. 2012. Applied longitudinal analysis. Vol. 998. John Wiley & Sons.) for continuous outcomes and generalized estimating equations logistic regression models (Preisser, J. S., Lohman, K. K., & Rathouz, P. J. 2002. Performance of weighted estimating equations for longitudinal binary data with drop-outs missing at random. Statistics in medicine, 21(20), 3035-305) for binary outcomes, including indicator

variables for time point, for treatment group, and for the interaction between the two (yielding treatment effects at 3 months and at 6 months). Owing to the balanced design, it will be possible to fit an unstructured correlation model to eliminate any sensitivity to correlation model misspecification.”

Reviewer 5 comment:

4. Since it uses EHR database, authors should raise and address the challenging issues of the EHR.

Author response: We concur that the EHR poses a critical barrier in implementation of health information technology (IT) and potential issues impacting implementation feasibility are important to explore. We are addressing challenges and potential facilitators associated with the EHR in both periodic reflections and stakeholder interviews.

Reviewer 5 comment:

5. It would be better to display the proposed hybrid study including clinical data and PRO measure. This will be helpful to understand the hybrid study.

Author response: We thank the Reviewer for this important point. We have endeavored to clarify how data will be integrated and used to inform future implementation efforts in the manuscript (page 15) and in response to item 2, above.

Reviewer 5 comment:

6. Since this study already started to recruit, some more description can be provided for the patient and public involvement in terms of design and feedback of the tool.

Author response: Thank you for your comment. Additional details about patient involvement in usability testing of the decision aid was added to the Methods (page 17). No additional patient and public involvement has taken place since the start of recruitment.

VERSION 2 – REVIEW

REVIEWER	Tan, Bryan National Healthcare Group Woodlands Health Campus, Orthopaedic Surgery
REVIEW RETURNED	02-Dec-2021
GENERAL COMMENTS	The authors have made a great effort to address all the concerns and queries raised up by all 5 reviewers and I am satisfied that the points raised have been addressed. The use of the SPIRIT checklist has ensured that this is a comprehensive protocol with all the key and relevant information provided.
REVIEWER	Bowden, Jocelyn The University of Sydney, Institute of Bone and Joint Research
REVIEW RETURNED	20-Nov-2021
GENERAL COMMENTS	I thank the authors for their comprehensive revisions. I have no further comments.